REMARKS

Currently, claims 64-88, including independent claim 64, are pending in the present application. Independent claim 64, for example, is directed to a method for detecting an analyte within a test sample. The method comprises providing a lateral flow assay device that comprises a porous membrane in fluid communication with phosphorescent particles conjugated with a specific binding member. The phosphorescent particles comprise a phosphorescent label encapsulated within a matrix, the phosphorescent label having an emission lifetime of about 1 microsecond or more. The porous membrane defines a detection zone within which is immobilized a capture reagent. The lateral flow assay device is contacted with the test sample. The detection zone is subject to pulses of illumination to generate a detection signal. The intensity of the detection signal is measured. The amount of the analyte within the test sample is proportional to the intensity of the detection signal.

In the Office Action, independent claim 64 was rejected under *35 U.S.C. §103(a)* as being obvious over Daniels, et al. (U.S. Patent Application Publication No. 2002/0004246) in view of O'Riordan, et al. (*Anal. Chem.,* **74** (2002) 5845-5850) and further in view of Klimant, et al. (U.S. Patent No. 6,770,220). Daniels, et al. is directed to a method for detecting an analyte. More specifically, the method employs semiconductor nanocrystals and microspheres dyed with semiconductor nanocrystals as detectable labels in a variety of biological and chemical formats, including immunochromatographic strip assays. As correctly noted by the Examiner, however, Daniels, et al. fails to disclose one or more limitations of the present claims. For example, Daniels, et al. does not disclose the use of phosphorescent particles that

comprise a phosphorescent label encapsulated within a matrix, the phosphorescent label having an emission lifetime of about 1 microsecond or more.

Nevertheless, O'Riordan, et al. was cited in combination with Daniels, et al. in an attempt to render obvious independent claim 64. More specifically, the Office Action cited O'Riordan, et al. for the teaching of a solid-phase immunoassay utilizing phosphorescent porphyrin labels that display high quantum yields, long phosphorescent lifetimes, and intense absorption bands.

Applicants respectfully submit that no teaching or motivation exists to combine the immunonochromatographic strip assays of Daniels, et al. with the phosphorescent porphyrin labels of O'Riordan, et al. to arrive at the limitations of independent claim 64. Though both references do utilize luminescent particles, the semiconductor nanocrystals of Daniels, et al. and the metalloporphyrins of O'Riordan, et al. are quite different with regard to many characteristics including luminescent properties. For example, the metalloporphyrins of O'Riordan, et al., as correctly pointed out in the Office Action, display intense absorption bands, Stokes' shifts greater than 100 nm, and phosphorescent lifetimes between 10 and 1000 μsec. In contrast, the semiconductor nanocrystals of Daniels, et al. have absorption wavelength and emission wavelengths near each other (see, e.g., paragraph [0086], in which the onset wavelength is near to that of the emission and Example 1, in which the excitation source is a 488 nm argon ion laser, and the emission spectra (shown in Figure 4) has an emission peak within 100 nm of the excitation wavelength). In addition, the emission lifetimes of semiconductor nanocrystals are in the range of nanoseconds or even picoseconds (see, e.g., *Phys. Rev. Lett.,* **86**:17 (2001) 3903-3906, and the product description for

Quantum Dots Fluor Labeling – Evident Technologies – Troy, NY USA, both of which are attached hereto at Appendix A and B, respectively) as compared to the extremely long emission lifetimes of the metalloporphyrins used by O'Riordan, et al.

The differences between the two references do not stop with the luminescent particles employed, however. For instance, Daniels, et al., which can be a flow-type assay device and can utilize a suitable absorbent, porous or capillary possessing material suitable thereto (paragraph [0126]). As such, the assay systems described in Daniels, et al. are dry chemistry-based devices. Moreover, Daniels, et al. utilizes a detection system suitable to both the semiconductor nanoparticles, the dry chemistry-based system and the construction materials (paragraphs [0170] – [0172]). For example, the detection system can include a light source of a wavelength shorter than that of the luminescence detected, imaging subtracting double monochromators including gratings or prisms, detectors to record the images, etc. Thus, the detection system of Daniels, et al. is effective to filter out the specific emission of the targeted nanocrystals from all of the other electromagnetic wavelengths present at the time, including light from the excitation source.

The system of O'Riordan, et al., in contrast, includes a time-resolved detection method and is carried out in a static system utilizing 96-well black microtiter plates (Experimental Section). In fact, the detection system of O'Riordan, et al. utilizes a *custom-designed instrument* (page 5846, first full paragraph, Figure 1) designed to be effective for use with the metalloporphyrin labels as well as with the well-plate design of the assay so as to obtain the desired time-resolved spectra. Moreover, the assay

system of O'Riordan, et al. is a solution chemistry-based system, rather than a dry chemistry-based system.

Applicant respectfully submits that there is no motivation to incorporate the system of O'Riordan, et al., which uses a *custom-designed instrument* specifically designed for time-resolved detection with the solution chemistry-based assay system, with the devices of Daniels, et al. in the specific manner required by independent claim 64. Porous membranes present a wide variety of problems for time-resolved phosphorescent detection. For example, many membranes, such as nitrocellulose membranes, exhibit strong fluorescence when excited in the UV and visible regions. This fluorescence may interfere with the accuracy of phosphorescence measurements, and in particular with detection during the emission lifetime of a phosphorescent label, as is required by independent claim 64. Such problems and conditions are neither encompassed nor addressed in the cited references. In light of the above, Applicant respectfully submits that one of ordinary skill in the art would not have found it obvious to make the combination proposed in the Office Action and that no reasonable expectation of success would have existed to make the combination proposed in the Office Action.

In the Office Action, Daniels, et al. was cited in view of O'Riordan, et al. and further in view of Klimant, et al. Specifically, Klimant, et al. was cited as teaching the production and use of luminescent microparticles wherein the phosphorescent labels are incorporated within solid particles.

O'Riordan, et al. generally describes phosphorescent porphyrin labels for use in solid-phase immunoassays of AFP. Applicant notes, however, that no motivation would

have existed to combine the teachings of O'Riordan, et al. and Klimant, et al. as suggested in the Office Action. Klimant, et al. is directed to the incorporation of phosphorescent substances into a solid matrix to shield them from interfering substances (e.g., O_2). In stark contrast, the phosphorescent labels of O'Riordan, et al. are not encapsulated, but instead simply mixed with Na_2SO_3 to eliminate interference by molecular oxygen and other quenchers (p. 5846). Due to the substantial differences in the fundamental construction and operation of the phosphorescent systems, one of ordinary skill in art would simply not have selectively picked and chosen certain aspects of O'Riordan, et al. for incorporation into Klimant, et al.

Applicant emphasizes that the issue in conducting an analysis under *35 U.S.C. § 103(a)* is not whether a theoretical re-design of a device is *possible* or that it might be *obvious to try* the modification. Instead, the issue hinges on whether the claimed invention as a whole would have been obvious. In this case, the Office Action parsed and dissected only certain portions of Klimant, et al. and O'Riordan, et al., and then used these dissected portions in a way that would require a substantial reconstruction of Daniels, et al. Clearly, the Office Action is using the present application as a "blueprint" for selectively re-designing the references, which is improper under *35 U.S.C. § 103*. Thus, for at least the reasons set forth above, Applicant respectfully submits that one of ordinary skill in the art would not have found it obvious to modify the references in the manner suggested in the Office Action.

It is believed that the present application is in complete condition for allowance and favorable action, therefore, is respectfully requested. Examiner DiRamio is invited

and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Amendment.

Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully requested,

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Date: 9/18/06